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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,624	01/27/2006	Alexander Ian Smith	DAVI-001/00US 040722-2001	5599

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COOLEY GODWARD KRONISH LLP
ATTN: Patent Group
Suite 1100
777 - 6th Street, NW
WASHINGTON, DC 20001

EXAMINER	
MA, JAMESON Q	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,624	SMITH ET AL.	
	Examiner	Art Unit	
	JAMESON Q. MA	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,15-21,23-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9,15-21,23-27 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 2, 4, 9, 15-21, 25-27, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jindal et al. (US 6,358,692).

Regarding claim 29, Jindal discloses a method for the detection of bioactive peptides derived from a precursor protein or protein-containing biological extract (see C1/L45-50 and C5/L35-39), comprising the steps of:

(i) providing a library of peptides derived from said precursor protein or protein-containing biological extract (see C1/L45-50 and C5/L35-39);

(ii) separating said library to provide fractions of the library (see C3/L27-29);

(iii) screening said fractions to identify active fractions which include peptides exhibiting said one or more target biological activities (see C3/L29-33: see "screening for second dimension");

(iv) isolating from said active fractions or active sub-fractions one or more peptides exhibiting said one or more target biological activities (Jindal teaches the screening of peptide libraries (see C28/L28-30), so the steps of eluting ligands having desired binding characteristics (see C3/L29-34) involves isolating peptides exhibiting one or more biological activities).

Regarding claims 30-31, Jindal discloses a method comprising the steps:

(v) optionally screening said library to confirm that it includes peptides exhibiting one or more target biological activities (see C3/L19-26: ligands having the first binding characteristic will bind to the target of interest reads on confirming biological activity);

(vi) optionally separating each said active fraction to provide sub-fractions thereof, and screening said sub-fractions to identify active sub-fractions which include peptides exhibiting said one or more target biological activities (see C3/L29-34);

Wherein said screening in step (v) and or (vi) is carried out using an assay which screens for said one or more target biological activities and wherein said fraction of step (vi) is carried out by chromatography (C3/L16-34 and C16/L33-58: since the target compounds represent specific biological activities such as agonist activity or antiviral activity, Jindal still discloses the method of screening for a biological activity).

Regarding claims 2 and 4, Jindal discloses all of the claim limitations as set forth above. Additionally, Jindal discloses the method wherein said library of peptides is derived by enzymatic cleavage or physical digestion (see C8/L1-4: enzymatic digestion reads on both enzymatic cleavage and physical digestion).

Regarding claim 9, Jindal discloses all of the claim limitations as set forth above. Additionally, Jindal discloses the method wherein said library of peptides is provided by chemical synthesis (see C1/L59-61).

Regarding claims 15-17, Jindal discloses all of the claim limitations as set forth above. Additionally, Jindal discloses the method wherein said precursor protein is:

- naturally occurring protein (see C8/L1: natural libraries).

- a non-naturally occurring protein (see C36/L6: a recombinant protein is a non-naturally occurring protein).
- a recombinant protein (see C36/L6).

Regarding claims 18-21, Jindal discloses all of the claim limitations as set forth above. Additionally, Jindal discloses the method wherein said biological activity:

- is agonist activity (see C16/L52).
- is antagonist activity (see C16/L52).
- relates to any human condition (see C6/L52: immune agonist/antagonist activity is inherently related to a human condition).
- relates to conditions selected from the group consisting of arterial and venous thrombosis, inflammation, angiogenesis and cancer (agonist activity is related to cancer, as evidenced by Spicer et al. (Future possibilities in the prevention of breast cancer Luteinizing hormone-releasing hormone agonists): see abstract).

Regarding claims 25-26, Jindal discloses all of the claim limitations as set forth above. Additionally, Jindal discloses the method wherein said fractionation step (ii) is carried out by:

- a fractionation method selected from the group consisting of chromatography, field flow fractionation and electrophoresis (see C3/L27-29: size exclusion is a form of column chromatography).
- chromatography (see C3/L27-29: size exclusion is a form of column chromatography).

Claim Rejections - 35 USC § 103

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (US 6,358,692) as applied to claim 29 above, in view of Smith (Chemical Cleavage of Polypeptides).

Regarding claim 3, Jindal discloses all of the claim limitations as set forth above. However, Jindal does not explicitly disclose the method wherein said library of peptides is derived by chemical cleavage of the precursor protein or protein-containing biological extract.

Smith teaches that chemical methods may be used to cleave proteins and peptides like endoproteolytic enzymes (see P57/L1-3).

Jindal and Smith are analogous because both references are directed to peptide cleavage.

It would have been obvious to one of ordinary skill at the time of invention to substitute for the step of enzyme cleavage of Jindal, chemical cleavage as taught by Smith, because doing so would have amounted to nothing more than the simple substitution of one known peptide cleavage method for another to obtain predictable results.

5. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (US 6,358,692) as applied to claim 29 above, in view of Herman et al.

(Optimization of the synthesis of peptide combinatorial libraries using a one pot method).

Regarding claims 5-7, Jindal teaches the use of libraries to screen for possible drug compounds (see C7/L57-62). Jindal also teaches the synthesis of a soluble peptide combinatorial library or SPCL (see C29/L23-24).

Jindal does not explicitly disclose the method wherein:

- said precursor protein or protein-containing biological extract, or said unfractionated peptide library is subjected to a determination of optimal cleavage conditions by monitoring the extent or progress of cleavage or digestion.
- said determination comprises mass spectometry analysis.
- said determination comprises MALDI-ToF MS analysis.

Herman teaches the use of combinatorial libraries to serve as a source of potential candidates in drug discovery (see P147/C1/L1-4). Herman also discloses that following the synthesis of SPCLs, MALDI-ToF mass spectrometry was used to judge the overall quality of the formed peptide libraries (see P148/C2/L5-15). Herman further discloses that the quality of a combinatorial peptide library is dependent upon the cleavage cocktail (see P149/C2/L29-33). Herman further teaches that samples cleaved with different reagents provided libraries with different amino acid balances (see P152/C1/L19-24).

Jindal and Herman are analogous because both references are directed to the synthesis of SPCLs for the purpose of drug discovery.

It would have been obvious to one of ordinary skill at the time of invention to optimize the SPCL synthesis method of Jindal, by MALDI-ToF analysis in order to optimize cleavage conditions as taught by Herman, in order to obtain a desired amino acid balance in the synthesized peptide library.

6. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (US 6,358,692) in view of Herman et al. (Optimization of the synthesis of peptide combinatorial libraries using a one pot method) as applied to claims 5-7 above, and further in view of Papac et al. (Mass spectrometry innovations in drug discovery and development).

Regarding claim 8, modified Jindal discloses all of the claim limitations as set forth above.

Further Herman teaches the use of MALDI-ToF in determining optimal cleavage conditions (see Herman P147/C1/L1-4, P148/C2/L5-15, P149/C2/L29-33, and P152/C1/L19-24). Modified Jindal does not explicitly disclose the method wherein said determination is automated.

Papac teaches that MALDI-ToF is capable of being automated for unattended protein identification for the purpose of minimizing operator involvement (see P138/C2/L1-3).

Modified Jindal and Papac are analogous because both references are directed to the use of MALDI-ToF for protein analysis.

It would have been obvious to one of ordinary skill at the time of invention to modify the method of using MALDI-ToF of modified Jindal, to incorporate automation as taught by Papac in order to reduce operator involvement.

7. Claims 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jindal et al. (US 6,358,692), as applied to claim 1 above, in view of Cree et al. (Measurement of cytotoxicity by ATP-based luminescence assay in primary cell cultures and cell lines).

Regarding claims 23-24, Jindal discloses all of the claim limitations as set forth above. Jindal teaches that compounds are screened for desired bioactivity by combining a solution of ligands to a target of interest to obtain information about binding characteristics (see C3/L17-25).

However, Jindal does not explicitly disclose the method:

- wherein said assay is selected from the group consisting of luminescence based assays for platelet activation, laser-based methods for Prothrombin Time and Activated Partial Thromboplastin Time, luminescence and fluorescence based detection of cell proliferation, cell toxicity and apoptosis and in vivo assays.
- wherein said assay is high throughput and automated.

Cree teaches a method of in vitro cell toxicity assay using the luciferin/luciferase reaction (see Abstract: luciferin/luciferase reaction is a luminescence method). Cree further teaches that toxicity is tested for the purpose of drug discovery and the assays can test four drugs/agents in triplicate (see Abstract and P553/C1/L19-P553/C2/L4).

Cree further teaches that the assays are conducted on 96-well microplates with 1000 cells/well for cell lines and 10000 cells/well for primary tumor tissue (see abstract: reads on high-throughput assay). Cree also teaches that the luminescence measurements are performed in a microplate luminometer (see P554/C2/L15-20: part of the assay performed in the luminometer is inherently automated).

Jindal and Cree are analogous because both references are directed to screening compounds for drug discovery.

It would have been obvious to one of ordinary skill at the time of invention to substitute for the target/ligand screening method of Jindal, the cytotoxicity screening method of Cree, because doing so would amount to nothing more than simple substitution of known methods for determining specific bioactivity in potential drug compounds, to accomplish expected results.

Response to Arguments

8. Applicant's arguments filed 1/30/2009 have been fully considered but they are not persuasive. Applicant gives a detailed explanation of the specification and how it differs from cited references in pages 9 through 13 of the response. Applicant further asserts the difference from the intended meaning of a true "biological" activity as opposed to a predetermined target molecule. It is noted that differences between the specifications of the instant application and the cited prior art do not distinguish the instant application from the prior art for patentability. Such differences must be recited in the claim language. Further applicant's amendment of the claims from "biological

activity" to "target biological activity" and applicant's assertion that Jindal does not teach such a limitation is noted but is not persuasive. Applicant states in page 11 of the response that a ligand selected by the method of Jindal does not necessarily correspond to a molecule having physiologically relevant “functional” activity. However it is noted that the target compounds in Jindal *can* have a desired target biological activity (see Jindal C16/L33-58). Therefore the cited reference meets the claim limitation of a 'target biological activity.' Applicant errs in stating that the “presently claimed invention is directed towards directly identifying functional target biological activity, without any prior knowledge or requirement of a pre-selected target of interest, and in fact independent of any pre-selected target of interest." There is no such limitation recited in the claim language. Applicant points to Jindal C2/L4-8 and states that Jindal emphasizes the distinction between use of screening assays directed toward identifying biological activity and ligand/target binding affinity approach and that this statement would not lead a person skilled in the art towards the invention. Again, it is noted that Jindal sufficiently describes that target ligands may have a desired biological activity and are still seen to meet the present limitations recited in the claims.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMESON Q. MA whose telephone number is (571)270-7063. The examiner can normally be reached on M-R 8:30 AM - 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JM

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797

April 14, 2009